

AMENDMENTS

IN THE CLAIMS

(33. (Currently Amended) A method of screening a substance substances for an ability to affect TRRE TNF receptor releasing activity, comprising:

a) incubating TNF receptor or cells expressing TNF receptor with the substance and with a polypeptide an isolated polypeptide that causes TNF receptor to be cleaved in the absence of the substance;

b) measuring any TNF receptor cleaved; and

c) correlating any increase or decrease of the receptor cleaved by the peptide polypeptide with an ability of the substance to enhance or diminish TRRE TNF receptor releasing activity ;

wherein the polypeptide has at least one of the following properties:

i) it comprises an amino acid sequence selected from SEQ. ID NOs: 151, 153, and 154;

ii) it comprises a fragment of any one of SEQ. ID NOs: 151, 153, or 154 that causes increased release of TNF receptor from human cells in which TNF receptor is expressed;

iii) it comprises an amino acid sequence encoded in any one of SEQ. ID NOs:1, 5, 6, 8, 9, or 10; or

iv) it comprises an amino acid sequence that causes increased release of TNF receptor from human cells in which TNF receptor is expressed, and is encoded by a polynucleotide that hybridizes-at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having a sequence selected from SEQ. ID NOs:1, 5, 6, 8, 9, or 10.

2 34. (Withdrawn) The screening method of claim ¹33, wherein the polypeptide contains SEQ. ID NOs: 147-149, 151, or 153-154, or fragment thereof which causes increased release of TNF receptor from human cells in which TNF receptor is expressed.

- 3 35. (Currently Amended) The screening method of claim 33, wherein the polypeptide has at least one of the following properties:
- i) it comprises a sequence encoded in the longest open reading frame of SEQ. ID NOs: ~~1-10~~ **or a fragment thereof 1, 5, 6, 8, 9, or 10 or fragment of any of these sequences; or**
 - ii) it is encoded by a polynucleotide that hybridizes at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having a sequence selected from SEQ. ID NOs: ~~1-10~~ **1, 5, 6, 8, 9, or 10;**
- and wherein the polypeptide causes increased release of TNF receptor from human cells in which TNF receptor is expressed.
- 4 36. (Previously Presented) The screening method of claim 33, wherein the polypeptide has been obtained by purifying TRRE from human cells that express it endogenously.
- 5 37. (Previously Presented) The screening method of claim 33, wherein the polypeptide has been obtained by expressing a recombinant polynucleotide.
- 6 38. (Previously Presented) The screening method of claim 33, wherein the polypeptide has metalloprotease activity.
- 7 39. (Currently Amended) The screening method of claim 35, wherein the polynucleotide comprises a sequence selected from the longest open reading frame of SEQ. ID NOs: ~~1-10 or fragment thereof 1, 5, 6, 8, 9, or 10, or a fragment of any of these sequences.~~
- 8 40. (Currently Amended) The screening method of claim 35, wherein the polynucleotide hybridizes ~~under stringent conditions at 30°C in 6 × SSC containing 50% formamide~~ to a polynucleotide having a sequence selected from SEQ. ID NOs: ~~1-10~~ **1, 5, 6, 8, 9, or 10, or a fragment of any of these sequences.**
- 9 AT. (Withdrawn) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:1 or fragment thereof.

- 10 42. (Withdrawn) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:5 or fragment thereof.
- 11 43. (Withdrawn) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:6 or fragment thereof.
- 12 44. (Withdrawn) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:8 or fragment thereof.
- 13 45. (Previously Presented) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:9 or fragment thereof.
- 14 46. (Withdrawn) The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:10 or fragment thereof.
- 15 47. (Withdrawn) (Currently Amended) The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:1.
- 16 48. (Withdrawn) (Currently Amended) The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:5.
- 17 49. (Withdrawn) (Currently Amended) The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:6.
- 18 50. (Withdrawn) (Currently Amended) The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:8.

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51. (Currently Amended) The screening method of claim 35 ~~33~~, wherein the polynucleotide hybridizes ~~under stringent conditions~~ at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:9.
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52. (Withdrawn) (Currently Amended) The screening method of claim 35 ~~33~~, wherein the polynucleotide hybridizes ~~under stringent conditions~~ at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:10.
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53. (Previously Presented) The screening method of claim ~~33~~, wherein the substance is incubated with p55 TNF receptor in step a).
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54. (Previously Presented) The screening method of claim ~~33~~, wherein the substance is incubated with p75 TNF receptor in step a).
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55. (Previously Presented) The screening method of claim ~~33~~, wherein the substance is incubated with a cell expressing p55 TNF receptor in step a).
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56. (Previously Presented) The screening method of claim ~~33~~, wherein the substance is incubated with a cell expressing p75 TNF receptor in step a).
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57. (Previously Presented) The screening method of claim ~~33~~, wherein the measuring of TNF receptor cleaved in step b) comprises measuring binding capacity for TNF on the surface of the treated cell.
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58. (Previously Presented) The screening method of claim ~~33~~, wherein the measuring of TNF receptor cleaved in step b) comprises measuring the concentration of soluble TNF receptor in culture medium from the treated cell.
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59. (New) The screening method of claim ~~33~~, wherein the polypeptide comprises SEQ. ID NO:151 or fragment thereof.

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60. (New) The screening method of claim ~~33~~¹, wherein the polypeptide comprises SEQ. ID NO:153
or fragment thereof.

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61. (New) The screening method of claim ~~33~~¹, wherein the polypeptide comprises SEQ. ID NO:154
or fragment thereof.